

EAST - [%default.wsp:1]

File View Edit Tools Window Help

Drafts
 BRS:
 BRS: 1 and 2
 Pending
 Active
 L1: (940578) conjugat\$4 or crosslink\$4 or link\$4
 L2: (408) (hbcag or hbsag) same 1
 L3: (234) (hbcag or hbsag) with 1
 Failed
 (0) s l3 and l4
 (0) 7 with 8
 Saved
 (31) FORMAT ADJ SAVE
 (31) molecular adj antigen
 (106) bachmann-m\$.in.
 (6922) hepatitis adj b or hbv
 (258450) core or nucleocapsid or hbcag
 (2209) (hepatitis adj b or hbv) and (core or nucleocapsid or hbcag)
 (1176) hbsag
 (1837627) hbsag or surface
 (940578) conjugat\$4 or crosslink\$4 or link\$4 or t
 (24189) (core or nucleocapsid or hbcag) with (cc)
 Favorites
 Tagged (10)
 UDC
 Queue
 Trash

Search List Processed Queued Details DBs USPAT Default operator: OR Plurals Highlight all hit terms initially

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments
1	BRS	L1	940578	conjugat\$4 or crosslink\$4 or link\$4 or bond\$4	USPAT	2003/01/31 13:53	
2	BRS	L2	408	(hbcag or hbsag) same 1	USPAT	2003/01/31 13:53	
3	BRS	L3	234	(hbcag or hbsag) with 1	USPAT	2003/01/31 13:53	

Hits Details HTML

EAST - [%default.wsp:1]

File View Edit Tools Window Help

Drafts
 BRS:
 BRS: 1 and 2

Pending

Active
 L1: (940578) conjugat\$4 or crosslink\$4 or link\$4
 L2: (408) (hbcag or hbsag) same 1
 L3: (234) (hbcag or hbsag) with 1

Failed
 (0) s l3 and l4
 (0) 7 with 8

Saved
 (31) FORMAT ADJ SAVE
 (31) molecular adj antigen
 (106) bachmann-m\$.in.
 (6922) hepatitis adj b or hbv
 (258450) core or nucleocapsid or hbcag
 (2209) (hepatitis adj b or hbv) and (core or nuc)
 (1176) hbsag
 (1837627) hbsag or surface
 (940578) conjugat\$4 or crosslink\$4 or link\$4 c
 (24189) (core or nucleocapsid or hbcag) with (conjuga

Favorites
 Tagged (10)

LINC

Search... Last... Browse... Recent... Open...
 DBs USPAT Plurals
 Default operator: OR Highlight all hit terms initially

BR5 IS... Image Text HTML

	Type	Hits	Search Text	DBs	Time Stamp
1	BRS	31	FORMAT ADJ SAVE	USPAT	2002/03/20 14:3
2	BRS	31	molecular adj antigen	EPO; JPO; DERWENT	2003/01/31 13:4
3	BRS	106	bachmann-m\$.in.	EPO; JPO; DERWENT	2003/01/31 13:4
4	BRS	6922	hepatitis adj b or hbv	USPAT	2003/01/31 13:4
5	BRS	258450	core or nucleocapsid or hbcag	USPAT	2003/01/31 13:4
6	BRS	2209	(hepatitis adj b or hbv) and (core or nucleocapsid or hbcag)	USPAT	2003/01/31 13:4
7	BRS	1176	hbsag	USPAT	2003/01/31 13:4
8	BRS	1837627	hbsag or surface	USPAT	2003/01/31 13:5
9	BRS	940578	conjugat\$4 or crosslink\$4 or link\$4 or bond\$4	USPAT	2003/01/31 13:5
10	BRS	24189	(core or nucleocapsid or hbcag) with (conjugat\$4 or crosslink\$4 or link\$4 or bond\$4)	USPAT	2003/01/31 13:5

? b 411

31jan03 14:27:30 User208669 Session D2201.1

\$0.32 0.093 DialUnits File1

\$0.03 TELNET

\$0.35 Estimated cost this search

\$0.35 Estimated total session cost 0.093 DialUnits

File 411:DIALINDEX(R)

DIALINDEX(R)

(c) 2003 The Dialog Corporation plc

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***

? sf allscience

You have 247 files in your file list.

(To see banners, use SHOW FILES command)

? s au=birkett? and hepatitis and core

Your SELECT statement is:

s au=birkett? and hepatitis and core

Items File

? b 5:exs
31jan03 14:29:07 User208669 Session D2201.2
\$3.33 1.905 DialUnits File411
\$3.33 Estimated cost File411
\$0.43 TELNET
\$3.76 Estimated cost this search
\$4.11 Estimated total session cost 1.998 DialUnits

File 5:Biosis Previews(R) 1969-2003/Jan W4
(c) 2003 BIOSIS
*File 5: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

Set Items Description

Executing TD791

557 AU=BIRKETT?

95405 HEPATITIS

65116 CORE

S1 8 AU=BIRKETT? AND HEPATITIS AND CORE

? t sl7/2 3
1/7/2

DIALOG(R)File 5:Biosis Previews(R)

(c) 2003 BIOSIS. All rts reserv.
13292576 BIOSIS NO.: 200100499725

Strategically modified hepatitis B core proteins and their derivatives.
AUTHOR: Birkett Ashley J(a)
JOURNAL: Official Gazette of the United States Patent and Trademark Office

Patents 1246 (3);pNo Pagination May 15, 2001
MEDIUM: e-file
ISSN: 0098-1133

DOCUMENT TYPE: Patent

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: A strategically modified hepatitis B core protein is described, where an insert is provided, preferably in an immunodominant region of the nucleocapsid protein, containing a chemically reactive amino acid residue. The modified hepatitis B core protein or its aggregated nucleocapsid protein particles can be pendently linked to a hapten to form a modified nucleocapsid conjugate. Such a conjugate is useful in the preparation of vaccines or antibodies. The modified hepatitis B core protein can also be modified to include a T cell epitope.

18 files have one or more items; file list includes 247 files.

One or more terms were invalid in 115 files.

? save temp

Temp SearchSave "TD791" stored

1/7/3

DIALOG(R)File 5:Biosis Previews(R)

(c) 2003 BIOSIS. All rts. reserv.

12637221 BIOSIS NO.: 200000390723

Immunization of mice with recombinant hepatitis B virus core (HBc) protein enhances the immunogenicity of variable domains of the major outer membrane protein of Chlamydia trachomatis.

AUTHOR: Peterson E M(a); Le V(a); Tapia O(a); de la Maza L M(a); Pal S(a); Birkett A

AUTHOR ADDRESS: (a)University of California, Irvine, CA**USA

JOURNAL: Abstracts of the General Meeting of the American Society for Microbiology 100p278 2000

MEDIUM: print

CONFERENCE/MEETING: 100th General Meeting of the American Society for Microbiology Los Angeles, California, USA May 21-25, 2000

SPONSOR: American Society for Microbiology

ISSN: 1060-2011

RECORD TYPE: Citation

LANGUAGE: English

SUMMARY LANGUAGE: English

? b 65,exs

31jan03 14:31:01 User208669 Session D2201.3

\$1.96 0.350 DialUnits File5

\$0.00 8 Type(s) in Format 6

\$3.50 2 Type(s) in Format 7

\$3.50 10 Types

\$5.46 Estimated cost File5

\$0.43 TELNET

\$5.89 Estimated cost this search
\$10.00 Estimated total session cost 2.348 DialUnits

File 65:Inside Conferences 1993-2003/Jan W4

(c) 2003 BLDSC all rts. reserv.

Set Items Description

Executing TD791

130 AU=BIRKETT?
5216 HEPATITIS
7894 CORE

S1 1 AU=BIRKETT? AND HEPATITIS AND CORE
? ts1/free

1/8/1
DIALOG(R)File 65:(c) 2003 BLDSC all rts. reserv. All rts. reserv.
03879396 INSIDE CONFERENCE ITEM ID: CN040776333
HEPATITIS B VIRUS CORE ANTIGEN PARTICLES CONTAINING MINIMAL T
AND B CELL

EPITOPES OF PLASMODIUM FALCIPARUM CS PROTEIN ELICIT HIGH LEVELS
OF MALARIA
SPECIFIC IMMUNE RESPONSES IN MICE AND NON-HUMAN PRIMATES

CONFERENCE: American Society of Tropical Medicine and Hygiene-Annual meeting, 50th (200111)

DESCRIPTORS: tropical medicine; hygiene; ASTMH
? b 35,exs

31jan03 14:31:33 User208669 Session D2201.4

\$0.86 0.229 DialUnits File65

\$0.00 1 Type(s) in Format 8

\$0.00 1 Types

\$0.86 Estimated cost File65

\$0.21 TELNET

\$1.07 Estimated cost this search

\$11.07 Estimated total session cost 2.577 DialUnits

File 35:Dissertation Abs Online 1861-2003/Jan
(c) 2003 ProQuest Info&Learning

Set Items Description
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Executing TD791

17 AU=BIRKETT?
831 HEPATITIS
23039 CORE

S1 1 AU=BIRKETT? AND HEPATITIS AND CORE
? ts1/6
1/6/1

01400687 ORDER NO: AAD95-06848
EXPRESSION, PURIFICATION AND CHARACTERIZATION OF HEPATITIS C
VIRUS CORE
PROTEIN FROM ESCHERICHIA COLI USING A CHEMICALLY SYNTHESIZED
GENE (1), AND
CLONING, EXPRESSION, PURIFICATION AND CHARACTERIZATION OF THE
MAJOR CORE
PROTEIN (P26) FROM EQUINE INFECTIOUS ANAEMIA VIRUS

Year: 1994
? ds

Set Items Description

S1 1 AU=BIRKETT? AND HEPATITIS AND CORE
? log hold

31jan03 14:32:06 User208669 Session D2201.5

\$0.93 0.227 DialUnits File35

\$0.00 1 Type(s) in Format 6

\$0.00 1 Types

\$0.93 Estimated cost File35

\$0.21 TELNET

\$1.14 Estimated cost this search

\$12.21 Estimated total session cost 2.804 DialUnits

Logoff: level 02.12.40 D 14:32:06

? b 155

31jan03 12:45:09 User2086669 Session D2200.1

\$0.39 0.112 DialUnits File

\$0.01 TELNET

\$0.40 Estimated cost this search

\$0.40 Estimated total session cost 0.112 DialUnits

File 155: MEDLINE(R) 1966-2003/Jan W4

*File 155: Updating of completed records has resumed. See Help News155.
 Alert feature enhanced with customized scheduling. See HELP ALERT.

Set Items Description

Set	Items	Description
S1	594330	PARTIC?
S2	5883	PLATFORM?
S3	80977	PRESENTING
S4	718	S1 AND S2
S5	6640	S1 AND S3
S6	300136	ANTIGEN
S7	12954	S6(W)S3
S8	1326	S1 AND S7
S9	329212	VIRUS OR VIRUSLIKE OR VLP
S10	187	S9 AND S8
S11	107300	HEPATITIS OR HBV
S12	18	S11 AND S10
S13	5094	NUCLEOCAPSID? OR HBCAG
S14	64911	CONJUGAT?
S15	43	S13 AND S14
S16	648188	CHEMICAL?
S17	175	S13 AND S16
S18	47	S11 AND S17
S19	107869	COUPLED OR COUPLING OR COUPLE
S20	9	S13 AND S19 AND S11
S21	7	S20 NOT S18
S22	9422	CROSSLINK?
S23	1	S11 AND S13 AND S22
S24	35	S11 AND S22

? t s12/7/11

DIALOG(R)File 155: MEDLINE(R)

13927589 22153991 PMID: 12163261

A molecular assembly system that renders antigens of choice highly repetitive for induction of protective B cell responses.

Jegerlehner Andrea; Tissot Alain; Lechner Franziska; Sebbel Peter;

Erdmann Iris; Kundig Thomas; Bachl Thomas; Storni Tazio; Jennings Gary;

Pumpens Paul; Renner Wolfgang A; Bachmann Martin F, et al

Cytos Biotechnology AG, CH-8952 Schlieren-Zurich, Switzerland.

Vaccine (England) Aug 19 2002, 20 (25-26) p3104-12, ISSN 0264-410X

California 92037, USA.

Annals of the New York Academy of Sciences (UNITED STATES) May 31 1995,
 754 p187-201, ISSN 0077-8923 Journal Code: 7506858
 Contract/Grant No.: AI 20720; AI; NIAID; AI 33562; AI; NIAID

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The "carrier effect," defined as the provision of T cell recognition sites physically linked to B cell epitopes in order to provide Th cell function for antibody synthesis, is well known. Peptides, proteins, and more recently particulate protein antigens have been used for this purpose.

The hepatitis B core antigen represents a highly immunogenic antigen in humans as well as in experimental animal models. Studies in mice have provided insight into this enhanced immunogenicity. For example, HBcAg directly activates B cells (i.e., T cell independence), HBcAg elicits strong T cell responses, and HBcAg is efficiently processed and presented by antigen presenting cells (APCs). These characteristics suggested that HBcAg may be an ideal carrier moiety for B cell epitopes requiring additional Th cell function. Therefore, a number of HBV and non-HBV B cell epitopes have been chemically linked or fused by recombinant methods to HBcAg as a method to increase immunogenicity with significant success. We have designed bacterial expression vectors that allow insertion of heterologous B cell epitopes at various positions within HBcAg particles and permit efficient purification of hybrid HBcAg particles. Studies of positional effects have demonstrated that an internal insertion into a dominant HBcAg-specific B cell site represents a superior location for enhanced antibody production. Immunogenicity studies have been extended to protection against experimental challenge in several systems. For example, a malaria CS repeat sequence derived from P. berghei was inserted into HBcAg at the internal site, and purified hybrid HBcAg/CS particles were highly immunogenic and protected 100% of experimentally challenged BALB/c mice. This system has also been exploited for purposes of oral vaccination by expressing genes coding for hybrid HBcAg particles in live, avirulent vaccine strains of *Salmonella* species.

Record Date Created: 19950825

? t s18/7/1 3 10
 18/7/1
 DIALOG(R)File 155: MEDLINE(R)
 A molecular assembly system that renders antigens of choice highly repetitive for induction of protective B cell responses.

Jegerlehner Andrea; Tissot Alain; Lechner Franziska; Sebbel Peter;
 Erdmann Iris; Kundig Thomas; Bachl Thomas; Storni Tazio; Jennings Gary;
 Pumpens Paul; Renner Wolfgang A; Bachmann Martin F, et al
 Cytos Biotechnology AG, CH-8952 Schlieren-Zurich, Switzerland.
 Vaccine (England) Aug 19 2002, 20 (25-26) p3104-12, ISSN 0264-410X

The hepatitis nucleocapsid as a vaccine carrier moiety.
 Milich D R; Peterson D L; Zheng J; Hughes J L; Wirtz R; Schodel F
 Department of Molecular Biology, Scripps Research Institute, La Jolla,

Journal Code: 8406899

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Process

Virus like particles (VLPs) are known to induce potent B cell responses in the absence of adjuvants. Moreover, epitope-specific antibody responses may be induced by VLPs that contain peptides inserted in their immunodominant regions. However, due to steric problems, the size of the peptides capable of being incorporated into VLPs while still permitting capsid assembly, is rather limited. While peptides genetically fused to either the N- or C-terminus of VLPs present fewer assembly problems, the immune responses obtained against such epitopes are often limited, most likely because the epitopes are not optimally exposed. In addition, such particles may be less stable in vivo. Here, we show that peptides and proteins engineered to contain a free cys can be chemically coupled to VLPs formed from the hepatitis B core antigen (HBcAg) containing a lys in the immuno-dominant region. By using this approach steric hindrance of capsid assembly is abrogated. Peptides or protein coupled to VLPs in an oriented fashion are shown to induce strong and protective B cell responses even against self-epitopes in the absence of adjuvants. This molecular assembly system may be used to induce strong B cell responses against most antigens.

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Record Date Created: 20020806

187/3
DIALOG(R)File 155: MEDLINE(R)
10853039 200404849 PMID: 10949916

Insertion of foreign epitopes in HBcAg: how to make the chimeric particle assemble.

Karpenko L I; Ivaniseiko V A; Pika I A; Chikatov N A; Eroshkin A M; Veremeiko T A; Il'yichev A A
Institute of Bioengineering, State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk Region, Russia.
karpenko@vector.nsk.su
Amino acids (AUSTRIA) 2000, 18 (4) p329-37, ISSN 0939-4451
Journal Code: 9200312
Document type: Journal Article

Record type: Completed
Languages: ENGLISH
Main Citation Owner: NLM

Hepatitis B core antigen is one of the most promising protein carriers of foreign epitopes of various human and animal pathogens. Chimeric HBcAg particles can be used as effective artificial immunogens. Unfortunately, not all chimeric proteins are able to be particulated. The dependence of correct or incorrect folding of chimeric proteins on physical and chemical properties of inserts was studied with the help of ProAnalyst, SALLX and

QSARPro computer programs. We have found that insertion of amino acids with high hydrophobicity, large volume, and high beta-strand index prevent self-assembling chimeric proteins. These factors are most important for the C-termini of inserts. Recommendations for obtaining correct folding of chimeric HBcAg particles have been given.

Record Date Created: 20001115

187/10
DIALOG(R)File 155: MEDLINE(R)
09738782 98181627 PMID: 9520999

Core particles of hepatitis B virus as carrier for foreign epitopes.

Ulrich R; Nassal M; Meissel H; Kruger D H
Charite Medical School, Humboldt University, Berlin, Germany.
Advances in virus research (UNITED STATES) 1998, 50 p141-82, ISSN 0065-3527 Journal Code: 0370441

Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM

Record type: Completed

To be effective as vaccines, most monomeric proteins and peptides either require chemical coupling to high molecular weight carriers or application together with adjuvants. More recently, recombinant DNA techniques have been used to insert foreign epitopes into proteins with inherent multimerization capacity, such as particle-forming viral capsid or envelope proteins. The core protein of hepatitis B virus (HBcAg), because of its unique structural and immunological properties, has gained widespread interest as a potential antigen carrier. Foreign sequences of up to approximately 40 amino acid residues at the N terminus, 50 or 100 amino acids in the central immunodominant c/e 1 epitope region of HBcAg, and up to 100 or even more residues at the C terminus, did not interfere with particle formation. The humoral immunogenicity of inserted epitopes is determined by the immunogenicity of the peptide itself and its surface exposure, and is influenced by the route of application. The probably flexible and surface-exposed c/e 1 region emerged as the most promising insertion site. When applied together with adjuvants approved for human and veterinary use, or even without adjuvants, such chimeric particles induced B and T cell immune responses against the inserted epitopes. In some cases neutralizing antibodies, cytotoxic T cells and protection against challenge with the intact pathogen were demonstrated. Major factors for the potentiated immune response against the foreign epitopes are the multimeric structure of chimeric HBcAg that results in a high epitope density per particle, and the provision of T cell help by the carrier moiety. Beyond its use as subunit vaccine, chimeric HBcAg produced in attenuated Salmonella strains may be applicable as live vaccine.

Record Date Created: 19980402
? save temp
Temp SearchSave "TD790" stored

? log hold
31jan03 13:01:59 User208669 Session D2200.2
\$9.59 2.996 DialUnits File155
\$0.00 117 Type(s) in Format 6
\$0.84 4 Type(s) in Format 7
\$0.84 121 Types
\$10.43 Estimated cost File155
\$3.68 TELNET
\$14.11 Estimated cost this search
\$14.51 Estimated total session cost 3.108 DialUnits
Logoff: level 02.12.40 D 13:01:59